



# PATENT SPECIFICATION

DRAWINGS ATTACHED

Inventor: DOUGLAS STEPHENSON

994742

Date of filing Complete Specification (under Section 3 (3) of the Patents Act 1949) Aug. 17, 1961.

Application Date: Sept. 9, 1960.

No. 31223/60.

Application Date: May 4, 1961.

No. 16180/61.

Complete Specification Published: June 10, 1965.

© Crown Copyright 1965.

Index at acceptance:—A5 B(2S, 3)

Int. Cl.:—A 61 k 3/78

## COMPLETE SPECIFICATION

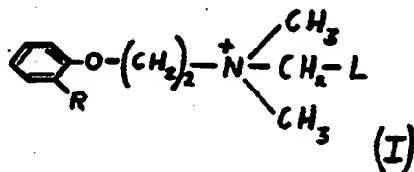
### Pharmaceutical Tablets containing Anthelmintics, and the Manufacture thereof

We, THE WELLCOME FOUNDATION LIMITED, a Company incorporated in England, 183—193 Euston Road, London, N.W.1, do hereby declare the invention for which we pray that a patent may be granted to us and the method by which it is to be performed to be particularly described in and by the following statement:—

The present invention relates to pharmaceutical compositions and to the manufacture thereof.

In both human and veterinary medicine an increasing interest is being taken in the treatment of helminth infections, particularly in the treatment of infections due to nematodes closely associated with the mucosa of the stomach and intestine. For this purpose there have been introduced into medical practice two types of salts: those of the *N*-benzyl-*N,N*-dimethyl-*N*-phenoxyethylammonium cation, which is commonly known as the "bephenium cation", and those of piperazine. Each of these types of salts is active against certain nematodes, though the respective ranges of activity are not identical. There has been much research and development into selecting salts which are most effective therapeutically and most convenient pharmaceutically; and each particular salt has its own advantages and disadvantages. Specific disadvantages of the salts of the bephenium cation are their bitter taste, their emetic effect and the effect of moisture on them, particularly on the readily soluble salts.

There are a number of quaternary ammonium cations related to the bephenium cation, whose salts exhibit the same activity and other properties. This whole group of quaternary ammonium cations is represented by the general formula (I):



In formula (I), R is a hydrogen, chlorine or bromine atom or a methyl or nitro group when L is a phenyl group optionally substituted in the *ortho* position with a chlorine, bromine or fluorine atom or a methyl group, or is a hydrogen or halogen atom or a methyl or nitro group when L is a thienyl group.

The present applicant has realised that there would be an advantage in providing a pharmaceutical composition containing both a salt of the bephenium cation (or of an analogous cation, as defined in formula (I)) and a salt of piperazine, and has arrived at a particularly advantageous composition.

According to the present invention in one aspect, there is provided a tablet comprising an inner portion, which contains a therapeutically acceptable quaternary ammonium salt having a cation of the formula (I) and an outer portion which completely surrounds the inner portion and contains a therapeutically acceptable salt of piperazine.